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L28: Entry 39 of 98 File: USPT Jul 11, 2000

DOCUMENT-IDENTIFIER: US 6086900 A
TITLE: Methods and compositions for using membrane-penetrating proteins to carry materials across cell membranes

Detailed Description Text (3):
In this regard, there are certain proteins that have the advantageous property of being able to pass through membranes into cells. Moreover, the proteins bind to receptors as a prerequisite for passing through a membrane which offers the opportunity to target only cells that have the receptors. These proteins, which will be termed hereafter as membrane-penetrating proteins (MPPs), include, but are not limited to, several plant and bacterial protein toxins, such as ricin, abrin, modeccin, diphtheria toxin, cholera toxin, anthrax toxin, heat labile toxins, and Pseudomonas aeruginosa exotoxin A (ETA). Examples of proteins that are not toxins but which appear to have properties of an MPP, include the TAT protein of human immunodeficiency virus (Frankel and Pabo, 1988; Mann and Frankel 1991) and the protein VP22, the product of the UL49 gene of herpes simplex virus type 1. One line of research involves adapting such molecules from their naturally destructive role into therapeutic compositions. If this can be accomplished, nature may have already provided a valuable starting point for the improvement of molecular therapies.

Detailed Description Text (12):
Exotoxin A (ETA) is a virulence factor and protein secreted by the bacteria Pseudomonas aeruginosa. ETA is the 66 kD protein product of the Pseudomonas aeruginosa toxA gene (SEQ ID NO:2, encoded by SEQ ID NO:1). The mature form of ETA has been subdivided into three domains, the receptor binding domain (domain I, residues 1-252 and 365-404), the membrane penetrating domain (domain II, residues 253-364), and the enzymatic ADP-ribosylation domain (Domain III, residues 405-613). The domains of ETA have been defined by x-ray crystallography (Allured et al. 1986) which shows that the functional domains overlap with the structural domains (FIG. 1).

Detailed Description Text (94):
Various toxins are also contemplated to be useful as part of the expression vectors of the present invention, these toxins include bacterial toxins such as ricin A-chain (Burbage, 1997), diphtheria toxin A (Massuda et al., 1997; Lidor, 1997), pertussis toxin A subunit, E. coli enterotoxin toxin A subunit, cholera toxin A subunit and pseudomonas toxin c-terminal. Recently, it was demonstrated that transfection of a plasmid containing the fusion protein regulatable diphtheria toxin A chain was cytotoxic for cancer cells. Thus, transfer of regulated toxin proteins might also be applied to the treatment of cancers (Massuda et al., 1997).

Detailed Description Text (201):
Allured et al., "Structure of exotoxin A of Pseudomonas aeruginosa at 3.0 angstrom resolution," Proc. Natl. Acad. Sci. USA, 83:1320-1324, 1986.

Detailed Description Text (205):

Benhar et al., "Pseudomonas exotoxin A mutants: replacement of surface-exposed residues in domain III with cysteine residues that can be modified with polyethyleme glycol in a site-specific manner," J. Biol. Chem., 269:13398-13404, 1994.

Detailed Description Text (211):
Chaudhary et al., "Pseudomonas exotoxin contains a specific sequence at the carboxyl terminus that is required for cytotoxicity," Proc. Natl. Acad. Sci. USA, 87:308-312, 1990.

Detailed Description Text (212):
Chaudhary et al., "A recombinant immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin," Nature, 339(6223):394-397, 1989.

Detailed Description Text (213):
Chiron et al., "Cleavage of Pseudomonas exotoxin and diphtheria toxin by a furin-like enzyme prepared from beef liver," J. Biol. Chem., 269:18167-18176, 1994.

Detailed Description Text (218):
Douglas and Collier, "Exotoxin A of Pseudomonas aeruginosa: substitution of glutamic acid 553 with aspartic acid drastically reduces toxicity and enzymatic activity," J. Bacteriol., 169(11):4967-4971, 1987.

Detailed Description Text (219):
Douglas et al., "Exotoxin A of Pseudomonas aeruginosa: active, cloned toxin is secreted into the periplasmic space of Escherichia coli," J Bacteriol., 169(11):4962-4966, 1987.

Detailed Description Text (221):
FitzGerald et al.,, "Receptor-mediated internalization of Pseudomonas toxin by mouse fibroblasts," Cell, 21(3):867-873, 1980.

Detailed Description Text (238):
Iglewski and Sadoff, "Toxin inhibitors of protein synthesis: production, purification, and assay of Pseudomonas aeruginosa toxin A," Methods Enzymol., 60:780-793, 1979.

Detailed Description Text (239):
Inocencio et al., "Furin activates Pseudomonas exotoxin A by specific cleavage in vivo and in vitro," J. Biol. Chem., 269:31831-31835, 1994.

Detailed Description Text (247):
Kounnas et al., "The 2-macroglobulin receptor/low density lipoprotein receptor-related protein binds and internalizes Pseudomonas exotoxin A," J. Biol. Chem., 267:12420-12423, 1992.

Detailed Description Text (256):
Lukac et al., "Toxoid of Pseudomonas aeruginosa exotoxin A generated by deletion of an active-site residue," Infect. Immun., 53:3095-3098, 1988.

Detailed Description Text (257):
Madshus and Collier, "Effects of eliminating a disulfide bridge within domain II of Pseudomonas aeruginosa exotoxin A," Infect. Immun., 57:1873-1878, 1989.

Detailed Description Text (263):
Moehring et al., "Expression of mouse furin in a Chinese hamster cell resistant to Pseudomonas exotoxin A and

viruses complements the genetic lesion," J. Biol. Chem., 268:2590-2594, 1993.

Detailed Description Text (267):
Ogata et al., "Processing of Pseudomonas exotoxin by a cellular protease results in the generation of a 37,000-Da toxin fragment that is translocated to the cytosol," J. Biol. Chem., 265:20678-20685, 1990.

Detailed Description Text (268):
Ogata et al., "Cell-mediated cleavage of Pseudomonas exotoxin between Arg.sup.279 and Gly.sup.280 generates the enzymatically active fragment which translocates to the cytosol," J. Biol. Chem., 267:25396-25401, 1992.

Detailed Description Text (274):
Prior et al., "Barnase toxin: a new chimeric toxin composed of Pseudomonas exotoxin A and barnase," Cell, 64:1017-1023, 1991.

Detailed Description Text (275):
Prior et al., "Translocation mediated by domain II of Pseudomonas exotoxin A: transport of barnase into the cytosol," Biochem., 31:3555-3559, 1992.

Detailed Description Text (287):
Siegall et al., "Functional analysis of domains II, Ib and III of Pseudomonas exotoxin," J. Biol. Chem., 264:14256-14261, 1989.

Other Reference Publication (2):
Benhar et al., "Pseudomonas exotoxin A mutants: replacement of surface-exposed residues in domain III with cysteine residues that can be modified with polyethyleme glycol in a site-specific manner," J. Biol. Chem., 269(18):13398-13404, 1994.

Other Reference Publication (6):
Chaudhary et al., "Pseudomonas exotoxin contains a specific sequence at the carboxyl terminus that is required for cytotoxicity," Proc. Natl. Acad. Sci. USA, 87:308-312, 1990.

Other Reference Publication (7):
Chaudhary et al., "A recombinant immunotoxin consisting of two antibody variable domains fused to Pseudomonas exotoxin," Nature, 339(6223):394-397, 1989.

Other Reference Publication (9):
Chiron et al., "Cleavage of Pseudomonas exotoxin and diphtheria toxin by a furin-like enzyme prepared from beef liver," J. Biol. Chem., 269:18167-18176, 1994.

Other Reference Publication (13):
Douglas and Collier, "Exotoxin A of Pseudomonas aeruginosa: substitution of glutamic acid 553 with aspartic acid drastically reduces toxicity and enzymatic activity," J. Bacteriol., 169(11):4967-4971, 1987.

Other Reference Publication (14):
Douglas et al., "Exotoxin A of Pseudomonas aeruginosa: active, cloned toxin is secreted into the periplasmic space of Escherichia coli," J. Bacteriol., 169(11):4962-4966, 1987.

Other Reference Publication (18):
Gray et al., "Cloning, nucleotide sequence, and expression in Escherichia coli of the exotoxin A structural gene of Pseudomonas aeruginosa," Proc. Natl. Acad. Sci. USA, 81:2645-2649, 1984.

Other Reference Publication (22):
Iglewski and Sadoff, "Toxin inhibitors of protein synthesis: production, purification, and assay of Pseudomonas aeruginosa toxin A," Methods Enzymol., 60:780-793, 1979.

Other Reference Publication (23):
Inocencio et al., "Furin activates Pseudomonas exotoxin A by specific cleavage in vivo and in vitro," J. Biol. Chem., 269:31831-31835, 1994.

Other Reference Publication (26):
Kounnas et al,. "The 2-macroglobulin receptor/low density lipoprotein receptor-related protein binds and internalizes Pseudomonas exotoxin A," J. Biol. Chem., 267:12420-12423, 1992.

Other Reference Publication (30):
Leppla, "Large-scale purification and characterization of the exotoxin of Pseudomonas aeruginosa," Infect. Immun., 14(4):1077-1086, 1976.

Other Reference Publication (33):
Lukac and Collier, "Restoration of enzymic activity and cytotoxicity of mutant, E553C, pseudomonas aeruginosa exotoxin A by reaction with iodoacetic acid," J. Biol. Chem. 263:6146-6149, 1988.

Other Reference Publication (34):
Lukac and Collier, "Pseudomonas aeruginosa exotoxin A: effects of mutating tyrosine-470 and tyrosine-481 to phenylalanine," Biochem., 27:7629-7632, 1988.

Other Reference Publication (35):
Lukac et al., "Toxoid of Pseudomonas aeruginosa exotoxin A generated by deletion of an active-site residue," Infect. Immun., 53:3095-3098, 1988.

Other Reference Publication (36):
Madshus and Collier, "Effects of eliminating a disulfide bridge within domain II of Pseudomonas aeruginosa exotoxin A," Infect. Immun., 57:1873-1878, 1989.

Other Reference Publication (39):
Moehring et al., "Expression of mouse furin in a Chinese hamster cell resistant to Pseudomonas exotoxin A and viruses complements the genetic lesion," J. Biol. Chem., 268:2590-2594, 1993.

Other Reference Publication (42):
Ogata et al., "Processing of Pseudomonas exotoxin by a cellular protease results in the generation of a 37,000-Da toxin fragment that is translocated to the cytosol," J. Biol. Chem., 265:20678-20685, 1990.

Other Reference Publication (43):
Ogata et al., "Cell-mediated cleavage of Pseudomonas exotoxin between Arg.sup.279 and Gly.sup.280 generates the enzymatically active fragment which translocates to the cytosol," J. Biol. Chem., 267:25396-25401, 1992.

Other Reference Publication (49):
Prior et al., "Barnase toxin: a new chimeric toxin composed of Pseudomonas exotoxin A and barnase," Cell, 64:1017-1023, 1991.

Other Reference Publication (50):

Prior et al., "Translocation mediated by domain II of Pseudomonas exotoxin A: transport of barnase into the cytosol," Biochem., 31(14):3555-3559, 1992.

Other Reference Publication (56):
Siegall et al., "Functional analysis of domains II, Ib and III of Pseudomonas exotoxin," J. Biol. Chem., 264:14256-14261, 1989.

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L7: Entry 10 of 37 File: USPT Aug 28, 2001

DOCUMENT-IDENTIFIER: US 6280975 B1
TITLE: IL-6 mutein and DNA encoding thereto

Brief Summary Text (10):
i. Epitope mapping of the IL-6 protein with neutralizing mAbs provided evidence that the residues Q152-T162 (beginning of the D-helix) are involved in gp130 interaction (17, 18). Analysis of chimeric human/mouse IL-6 proteins revealed the presence of an epitope within the beginning of the A-B loop of IL-6 which was involved in contacting and activating gp130 (9, 19). Recently, this result was confirmed by demonstrating that leucine 57 is invoved in this interaction (20). This region is in close proximity of the beginning of helix D leading to the assumption that these two regions together form a common interaction site with one gp130 (9, 19, 21).

Detailed Description Text (35):
K54, however, is believed to be one of the surrounding residues of a central IL-6/gp130 interaction area which therefore contributes to a small extent to the binding energy. The relatively strong effect of the K54P substitution in the antagonistic IL-6 mutein is attributed to structural changes in the AB-loop.

Detailed Description Text (37):
So far two major regions of IL-6 have been identified which are believed to contact gp130, (i) the 2a2 region (residues 50-55) and leucine 57 which are complemented by the top of the helix D of IL-6 and (ii) an epitope which is formed by parts of helix A and helix C (9, 18-21, 23, 24). Binding of IL-6 to the IL-6Ra requires the end of the A-B loop (residue 78) as well as the C-terminus of the protein (9, 13-16). It is clear that two gp130 molecules are necessary for signal initiation and it is very likely that the role of the two gp130 interaction sites within IL-6 is to engage the two gp130 proteins. Alterations within both gp130 interacting regions have led to molecules which retained their receptor binding capacity but failed to initiate signaling. It has been shown that such molecules can be used as IL-6 receptor antagonists (19, 21, 23, 24). The fact that simultaneously improving the IL-6Ra binding characteristics of IL-6 muteins has led to so-called superantagonists (19, 21, 24) suggesting that it is possible to change binding properties to various receptor subunits in a somehow independent fashion.

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L7: Entry 28 of 37 File: USPT Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723120 A
TITLE: Method of treating an IL-6 related disease with interleukin-6 receptor antagonists

Brief Summary Text (7):
Mature human (h) IL-6 is a 185 amino acid polypeptide containing two disulfide bonds (Cys.sub.45 to Cys.sub.51 and Cys.sub.74 to Cys.sub.84). Clogston et al., Arch. Biochem. Biophys. (1989) 272:144. The first 28 residues can be deleted without affecting bioactivity. Brakenhoff et al., J. Immunol. (1989) 143:1175. Bioactivity of hIL-6 appears to be conformation dependent. Large internal deletions disrupt the overall structure of the molecule and completely abolish activity. Snouwaert et al., J. Immunol. (1991) 146:585; and Fontaine et al., Gene (1991) 104:227. Maintenance of the second (but not the first) disulfide bond is critical, especially in bioassays involving human cell lines. Snouwaert et al., J. Biol. Chem. (1991) 266:23097. Regions critical to activity comprise residues Ile.sub.30 to Asp.sub.35 (see Brakenhoff et al., supra; Fontaine et al., supra; and Arcone et al., FEBS Letters (1991) 288:197), Ala.sub.154 to Thr.sub.164 (see Ida et al., Biochem, Biophys. Res. Commun. (1991) 165:728; and Nishimura et al., FEBS Letters (1991) 281:167) and Arg.sub.183 to Met.sub.183 (see Kruttgen et al., FEBS Letters (1990) 262:323; Brakenhoff et al., J. Immunol. (1990) 145:561; and Kruttgen et al., FEBS Letters (1990) 273:95). Substitution analysis of individual residues have implicated Leu.sub.159, Met.sub.162 and Leu.sub.166 to be important both for activity and binding to IL-6R (see Nishimura et al., supra). A positive charge and .alpha.-helical C-terminal structure were found to be essential for activity. Lutticken et al., FEBS Letters (1991) 282:265.

Other Reference Publication (26):
Clogston et al., "Disulfide Structures of Human Interleukin-6 Are Similar to Those of Human Granulocyte Colony Stimulating Factor", Arch. Biochem. Biophys., 272(1):144-151 (1989).

Other Reference Publication (75):
Snouwaert et al., "Role of Disulfide Bonds in Biologic Activity of Human Interleukin-6", J. Biol. Chem., 266:23097-23102 (1991).

WEST Search History

DATE: Tuesday, July 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=AND		
L1	((((kdel or sekdel or redlk or redl)and (((loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2))and endoplasmic)and (translocat$ or endocyto$ or poreform$)))and loop) and (receptor or cellbinding or recognition or targeting or targeted))	17	L1
L2	6498233.pn. and loop	1	L2
L3	L2 and (ib or lb or 1b or i-b or l-b or 1-b)	1	L3
L4	5935580.pn. and endoplasmic	1	L4
L5	multidomain.clm.	31	L5
L6	6022950.pn. and (hlh or loop or cys-cys)	1	L6
L7	L6 and l1	0	L7
L8	L6 and reticulum	0	L8
L9	L6 and endoplasmic	0	L9
L10	L6 and retension	0	L10
L11	L6 and epitope	0	L11
L12	L6 and antigen	1	L12
L13	loop same (foreign or heterologous or hetero-logous or nonnative or non-native)	1223	L13
L14	L13 and binding and translocation and (reticulum or retension or retention or kdel or sekdel or redl or redelk)	57	L14

L15	kdel or sekdel or redlk or redl	769	L15
L16	L15 and (moiety or moieties or domain or domains or portion or portions or region or regions)	624	L16
L17	loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2)	1469	L17
L18	L17 and l16	22	L18
L19	((loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2)) and ((kdel or sekdel or redlk or redl)and (moiety or moieties or domain or domains or portion or portions or region or regions)))	22	L19
L20	hiv.clm. and loop.clm. and heterologous.clm.	7	L20
L21	(hiv.clm. and loop.clm. and heterologous.clm.)	7	L21
L22	pastan.in. and loop	16	L22
L23	pastan.in. and hiv	7	L23
L24	pastan.in. and (v3 or v-3)	0	L24
L25	pastan.in. and (hiv same loop)	0	L25
L26	domain near5 1b	471	L26
L27	L26 and pseudomon$	41	L27
L28	((ib or lb or 1b or i-b or l-b or 1-b) near5 domain) and pseudomon$	98	L28
L29	6083502.pn.	1	L29
L30	(((ib or lb or 1b or i-b or l-b or 1-b) near5 domain) and pseudomon$)	98	L30

END OF SEARCH HISTORY

WEST Search History

DATE: Tuesday, July 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=AND		
L1	((((kdel or sekdel or redlk or redl)and (((loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2))and endoplasmic)and (translocat$ or endocyto$ or poreform$)))and loop) and (receptor or cellbinding or recognition or targeting or targeted))	17	L1
L2	6498233.pn. and loop	1	L2
L3	L2 and (ib or lb or 1b or i-b or l-b or 1-b)	1	L3
L4	5935580.pn. and endoplasmic	1	L4
L5	multidomain.clm.	31	L5
L6	6022950.pn. and (hlh or loop or cys-cys)	1	L6
L7	L6 and l1	0	L7
L8	L6 and reticulum	0	L8
L9	L6 and endoplasmic	0	L9
L10	L6 and retension	0	L10
L11	L6 and epitope	0	L11
L12	L6 and antigen	1	L12
L13	loop same (foreign or heterologous or hetero-logous or nonnative or non-native)	1223	L13
L14	L13 and binding and translocation and (reticulum or retension or retention or kdel or sekdel or redl or redelk)	57	L14

L15	kdel or sekdel or redlk or redl	769	L15
L16	L15 and (moiety or moieties or domain or domains or portion or portions or region or regions)	624	L16
L17	loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2)	1469	L17
L18	L17 and l16	22	L18
L19	((loop same (antigen or epitope or mimeotope or immunogen or immunogenic or antigenic or bcell or tcell or th1 or th2)) and ((kdel or sekdel or redlk or redl)and (moiety or moieties or domain or domains or portion or portions or region or regions)))	22	L19

END OF SEARCH HISTORY

The Canadian and Korean ExPASy sites, **ca.expasy.org** and **kr.expasy.org**, are temporarily not available.

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[Entry info] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**Q9GYZ2**
Primary accession number	**Q9GYZ2**
Secondary accession numbers	None
Entered in TrEMBL in	Release 16, March 2001
Sequence was last modified in	Release 16, March 2001
Annotations were last modified in	Release 24, June 2003

Name and origin of the protein

Protein name	**Monoclonal anti-idiotypic antibody NP30 heavy chain variable region [Fragment]**
Synonyms	None
Gene name	None
From	Schistosoma japonicum (Blood fluke) [TaxID: 6182]
Taxonomy	Eukaryota; Metazoa; Platyhelminthes; Trematoda; Digenea; Strigeidida; Schistosomatoidea; Schistosomatidae; Schistosoma.

References

[1] SEQUENCE FROM NUCLEIC ACID.
Song X.T., Feng Z.Q., Guan X.H.;
"Amplification, cloning and sequence analysis of the heavy chain variable region gene of monoclonal anti-idiotypic antibody NP30 of Schistosoma japonicum.";
Submitted (JUN-2000) to the EMBL/GenBank/DDBJ databases.

Comments

None

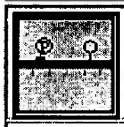
Cross-references

EMBL	AF282622; AAG01452.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
HSSP	P01772; 2FB4. [HSSP ENTRY / PDB]
InterPro	IPR007110; Ig-like. IPR003596; Ig_v. Graphical view of domain structure.
Pfam	PF00047; ig; 1.
SMART	SM00406; IGv; 1.
ProtoMap	Q9GYZ2.
PRESAGE	Q9GYZ2.
ModBase	Q9GYZ2.
SWISS-2DPAGE	Get region on 2D PAGE.

Keywords

None

Features



Feature table viewer

Key	From	To	Length	Description
NON_TER	1	1		
NON_TER	119	119		

Sequence information

Length: **119 AA** [This is the length of the partial sequence]	Molecular weight: **13567 Da** [This is the MW of the partial sequence]	CRC64: **BA893873FD5FA6AB** [This is a checksum on the sequence]

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QVQLVESGAE VRKPGASVRV SCKASGYTFT GYYMNWVRQA PGHGLEWIGY INPSRGYTNY

         70         80         90        100        110
          |          |          |          |          |
NQKFKDRVTM TTDKSFSTAY MDLRSLRSAD SAVYYCARYY DDHYCLDYWG QGTTVTVSS
```

Q9GYZ2 in FASTA format

View entry in original TrEMBL format
View entry in raw text format (no links)
Request for annotation of this TrEMBL entry

BLAST BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Search the SWISS-MODEL Repository

The Canadian and Korean ExPASy sites, **ca.expasy.org** and **kr.expasy.org**, are temporarily not available.

NiceProt View of Swiss-Prot: P01741

Printer-friendly view | Quick BlastP search

[Entry info] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**HV00_MOUSE**
Primary accession number	**P01741**
Secondary accession numbers	None
Entered in Swiss-Prot in	Release 01, July 1986
Sequence was last modified in	Release 01, July 1986
Annotations were last modified in	Release 42, September 2003

Name and origin of the protein

Protein name	**Ig heavy chain V region**
Synonym	**Anti-arsonate antibody**
Gene name	None
From	Mus musculus (Mouse) [TaxID: 10090]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

References

[1] SEQUENCE.
STRAIN=A/J;
MEDLINE=79195438; PubMed=109536; [NCBI, ExPASy, EBI, Israel, Japan]
Capra J.D., Nisonoff A.;
"Structural studies on induced antibodies with defined idiotypic specificities. VII. The complete amino acid sequence of the heavy chain variable region of anti-p-azophenylarsenate antibodies from A/J mice bearing a cross-reactive idiotype.";
J. Immunol. 123:279-284(1979).

Comments

- ***MISCELLANEOUS***: ANTIBODY ISOLATED FROM TEN MICE WAS EXCLUSIVELY OF THE IGG1 SUBCLASS. THERE WAS NO HETEROGENEITY IN THE HEAVY CHAIN V REGION SEQUENCE.
- ***SIMILARITY***: Contains 1 immunoglobulin-like domain.

Cross-references

PIR	A02022; G1MSAA.
HSSP	P01772; 2FB4. [HSSP ENTRY / PDB]
Ensembl	P01741; Mus musculus. [Entry / Contig view]
InterPro	IPR007110; Ig-like. IPR003596; Ig_v. Graphical view of domain structure.
Pfam	PF00047; ig; 1.
SMART	SM00406; IGv; 1.
PROSITE	PS50835; IG_LIKE; 1.
HOVERGEN	[Family / Alignment / Tree]
BLOCKS	P01741.
ProtoNet	P01741.
ProtoMap	P01741.
PRESAGE	P01741.
DIP	P01741.
ModBase	P01741.
SWISS-2DPAGE	Get region on 2D PAGE.

Keywords

Immunoglobulin V region.

Features

Feature table viewer

Key	From	To	Length	Description
DOMAIN	1	106	106	IG-LIKE.
NON_TER	114	114		

Sequence information

Length: **114 AA** [This is the length of the partial sequence]	Molecular weight: **12555 Da** [This is the MW of the partial sequence]	CRC64: **99DD8F0B6A69F4BE** [This is a checksum on the sequence]

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EVQLQQSGAE LVKAGSSVKM SCKATGYTFS SYELYWVRQA PGQGLEDLGY ISSSSAYPNY

         70         80         90        100        110
          |          |          |          |          |
AQKFQGRVTI TADESTNTAY MELSSLRSED TAVYFCAVRV ISRYFDGWGQ GTLV
```

P01741 in FASTA format

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Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Search the SWISS-MODEL Repository

ExPASy Home page | Site Map | Search ExPASy | Contact us | Swiss-Prot

Hosted by NCSC US | Mirror sites: Bolivia | China | Switzerland | Taiwan

The Canadian and Korean ExPASy sites, **ca.expasy.org** and **kr.expasy.org**, are temporarily not available.

The Canadian and Korean ExPASy sites, **ca.expasy.org** and **kr.expasy.org**, are temporarily not available.

Search Swiss-Prot/TrEMBL for Go Clear

NiceProt View of TrEMBL: Q9U410

Printer-friendly view | Quick BlastP search

[Entry info] [Name and origin] [References] [Comments] [Cross-references] [Keywords] [Features] [Sequence] [Tools]

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**Q9U410**
Primary accession number	**Q9U410**
Secondary accession numbers	None
Entered in TrEMBL in	Release 13, May 2000
Sequence was last modified in	Release 13, May 2000
Annotations were last modified in	Release 24, June 2003

Name and origin of the protein

Protein name	**Monoclonal anti-idiotypic antibody NP30 immunoglobulin light chain variable region [Fragment]**
Synonyms	None
Gene name	None
From	Schistosoma japonicum (Blood fluke) [TaxID: 6182]
Taxonomy	Eukaryota; Metazoa; Platyhelminthes; Trematoda; Digenea; Strigeidida; Schistosomatoidea; Schistosomatidae; Schistosoma.

References

[1] SEQUENCE FROM NUCLEIC ACID.
Song X.T., Feng Z.Q., Qiu Z.N., Li Y.Q., Huang H.L., Guan X.H.;
"Amplification, cloning and sequence analysis of the light chain variable region gene of monoclonal anti-idiotypic antibody NP30 of Schistosoma japonicum.";
Submitted (NOV-1999) to the EMBL/GenBank/DDBJ databases.

Comments

None

Cross-references

EMBL	AF207620; [EMBL / GenBank / DDBJ] AAF19434.1; -. [CoDingSequence]
HSSP	P01679; 2FBJ. [HSSP ENTRY / PDB]
InterPro	IPR007110; Ig-like. IPR003596; Ig_v. Graphical view of domain structure.
Pfam	PF00047; ig; 1.
SMART	SM00406; IGv; 1.
ProtoMap	Q9U410.
PRESAGE	Q9U410.
ModBase	Q9U410.
SWISS-2DPAGE	Get region on 2D PAGE.

Keywords

None

Features

Feature table viewer

Key	From	To	Length	Description
NON_TER	1	1		
NON_TER	106	106		

Sequence information

Length: **106 AA** [This is the length of the partial sequence]	Molecular weight: **11478 Da** [This is the MW of the partial sequence]	CRC64: **F20F544426BAE63E** [This is a checksum on the sequence]

```
         10         20         30         40         50         60
         |          |          |          |          |          |
ENLLTQSPAI MSASPGEKVT MTCSASSSVS YVYWYLQKPG SSPRLLIYDT SNLASGVPVR

         70         80         90        100
         |          |          |          |
FSGSGSGTSY SLTISRMEAE DAATYYCQQW TSYPFTFGSG TKLELK
```

Q9U410 in FASTA format

View entry in original TrEMBL format
View entry in raw text format (no links)
Request for annotation of this TrEMBL entry

BLAST BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Search the SWISS-MODEL Repository

ExPASy Home page | Site Map | Search ExPASy | Contact us | Swiss-Prot

Hosted by NCSC US | Mirror sites: Bolivia | China | Switzerland | Taiwan

The Canadian and Korean ExPASy sites, **ca.expasy.org** and **kr.expasy.org**, are temporarily not available.

WEST Search History

updated search 7/03 BP

DATE: Tuesday, July 29, 2003

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=AND		
L1	gp120.clm. or gp-120.clm.	223	L1
L2	L1 and (exotoxin or exo-toxin or cytotoxin or cyto-toxin or pseudomonas).clm.	5	L2
L3	(gp120 or gp-120 or v3) same (pseudomonas or pea or pe or exotoxin or exo-toxin or cytotoxin or cyto-toxin)	102	L3
L4	L3 and (insert$ or substitut$)	86	L4
L5	L4 and (1b or ib or lb or 1-b or i-b or l-b)	49	L5
L6	(il6 or il-6 or interleukin6 or interleukin-6) same (disulfide or loop or hlh)	101	L6
L7	(il6 or il-6 or interleukin6 or interleukin-6) near25 (disulfide or loop or hlh)	37	L7

END OF SEARCH HISTORY

WEST

Generate Collection

L28: Entry 50 of 98 File: USPT Jan 4, 2000

DOCUMENT-IDENTIFIER: US 6011002 A
TITLE: Circularly permuted ligands and circularly permuted chimeric molecules

Brief Summary Text (5):
Where the first constituent molecule is a ligand and the second protein is a cytotoxin, the chimeric molecule may act as a potent cell-killing agent specifically targeting the cytotoxin to cells bearing a particular receptor type. For example, chimeric fusion proteins which include interleukin 4 (IL4) or transforming growth factor (TGF.alpha.) fused to Pseudomonas exotoxin (PE) or interleukin 2 (IL2) fused to Diphtheria toxin (DT) have been tested for their ability to specifically target and kill cancer cells (Pastan et al., Ann. Rev. Biochem., 61: 331-354 (1992)).

Drawing Description Text (21):
The term "Pseudomonas exotoxin" (PE) as used herein refers to a full-length native (naturally occurring) PE or a PE that has been modified. Such modifications may include, but are not limited to, elimination of domain Ia, various amino acid deletions in domains II and III, single amino acid substitutions (e.g., replacing Lys with Gln at positions 590 and 606), and the addition of one or more sequences at the carboxyl terminus such as KDEL (SEQ ID NO:62) and REDL (SEQ ID NO:60).

Drawing Description Text (23):
All amino acid positions described herein use as a frame of reference sequences for native Pseudomonas exotoxin (PE) (SEQ ID NO:1), IL4 (SEQ ID NO:2), IL2 (SEQ ID NO:3), GM-CSF (SEQ ID NO:4), G-CSF (SEQ ID NO:5) as presented in the Sequence Listing. For example, a PE molecule "comprising amino acids 280 to 613" would refer to a molecule having amino acids substantially corresponding to those positions in SEQ ID NO:1. Other common references are used herein to indicate deletions or substitutions to a sequence using the respective native sequence Id. listing as a frame of reference. The use of the symbol ".DELTA." refers to a deletion of the amino acids following the symbol. For example, ".DELTA.365-380", refers to the deletion from a PE molecule of amino acids 365 to 380. Amino acid substitutions may be indicated by parentheses, for example "(Ser 287)" refers to a molecule having serine at amino acid position 287. Circularly permuted molecules are designated by the native molecule followed by brackets enclosing the amino acid positions that comprise the opening site. Thus, for example, IL4(105-104) designates a circularly permuted IL4 in which the new termini are residues 105 and 104 of the unpermuted IL4. Amino acids are also sometimes referred to here by the single letter codes recommended by the IUPAC-IUB Biochemical Nomenclature commission. It is, of course, recognized that some substitutions, addition, or deletions may be made to any sequences described herein that do not alter the biological activity of the region. Indeed, some such modifications may be required to achieve expression of a particular protein. Thus, for example, a methionine may be added to a sequence to provide an initiator.

Drawing Description Text (80):
Generally, the spacer has no biological activity itself and functions only to link and provide some distance

between the two active proteins comprising the fusion protein. However, one of skill will recognize that the residues of the spacer may be chosen to optimize a property of the fusion protein. For example, a spacer containing hydrophobic amino acids may enhance the solubility of the fusion protein in various lipids, while polar or charged residues in the spacer may enhance solubility in aqueous solutions. Similarly, the spacer residues may be chosen for their effect on the folding of the fusion protein. Where the fusion protein comprises a circularly permuted IL4, IL2, GM-CSF, or G-CSF joined to a Pseudomonas exotoxin a preferred peptide spacer is ASGGPE (SEQ ID NO:57). Where the last amino acid of the protein is alanine (as in IL4(105-104)), the protein and spacer may share the alanine. Where the fusion protein comprises a circularly permuted IL4 joined to Diptheria toxin DT388 preferred spacers are HM or RPHMAD (SEQ ID NO:53). Where the fusion protein comprises circularly permuted IL4 joined to an B3(Fv), a preferred spacer is ASGGPE (SEQ ID NO:57).

Drawing Description Text (82):
Chimeric ligand-toxin molecules are of particular interest and comprise a circularly permuted ligand joined to a toxin. Particularly preferred are chimeric toxin fusion proteins. One of skill in the art would recognize that many toxins are suitable including Pseudomonas exotoxin, Diphtheria toxin, other bacterial toxins, and derivatives of plant or animal toxins. In a preferred embodiment, the fusion protein comprises a circularly permuted growth-factor fused to either a Pseudomonas exotoxin or a Diphtheria toxin.

Drawing Description Text (83):
Pseudomonas exotoxin A (PE) is an extremely active monomeric protein (molecular weight 66 kD), secreted by Pseudomonas aeruginosa, which inhibits protein synthesis in eukaryotic cells through the inactivation of elongation factor 2 (EF-2) by catalyzing its ADP-ribosylation (catalyzing the transfer of the ADP ribosyl moiety of oxidized NAD onto EF-2).

Drawing Description Text (84):
The toxin contains three structural domains that act in concert to cause cytotoxicity. Domain Ia (amino acids 1-252) mediates cell binding. Domain II (amino acids 253-364) is responsible for translocation into the cytosol and domain III (amino acids 400-613) mediates ADP ribosylation of elongation factor 2, which inactivates the protein and causes cell death. The function of domain Ib (amino acids 365-399) remains undefined, although a large part of it, amino acids 365-380, can be deleted without loss of cytotoxicity. See Siegall et al., J. Biol. Chem. 264: 14256-14261 (1989), incorporated by reference herein. For example, in the case of B3(Fv)PE38 (described below), residues 350 to 394 can be deleted and if replaced with GGGGS SEQ ID NO:54) are fully active.

Drawing Description Text (85):
Where the circularly permuted ligand is fused to PE, i preferred PE molecule is one in which domain Ia (amino acids 1 through 252) is deleted and amino acids 365 to 380 have been deleted from domain Ib. However all of domain Ib and a portion of domain II (amino acids 350 to 394) can be deleted, particularly if the deleted sequences are replaced with a linking peptide such as GGGGS (SEQ ID NO:54).

Drawing Description Text (88):
Deletions of amino acids 365-380 of domain Ib can be made without loss of activity. Further, a substitution of methionine at amino acid position 280 in place of glycine to allow the synthesis of the protein to begin and of serine at amino acid position 287 in place of cysteine to prevent formation of improper disulfide bonds is beneficial. In a preferred embodiment, the circularly permuted ligand is inserted in replacement for domain Ia. A similar insertion has been accomplished in what is known as the TGF.alpha./PE40 molecule (also referred to as TP40) described in Heimbrook et al., Proc. Natl. Acad. Sci., U.S.A., 87: 4697-4701 (1990) and in commonly assigned U.S. Ser. No. 07/865,722 filed Apr. 8, 1992 now abandoned and in U.S. Ser. No. 07/522,563 filed May 14, 1990 now U.S. Pat. No. 5,458,878, all of which are incorporated by reference.

Drawing Description Text (92):
The circularly permuted ligand may also be inserted at a point within domain III of the PE molecule. Most preferably the circularly permuted ligand is fused between about amino acid positions 607 and 609 of the PE molecule. This means that the circularly permuted ligand is inserted after about amino acid 607 of the molecule and an appropriate carboxyl end of PE is recreated by placing amino acids about 604-613 of PE after the circularly permuted ligand. Thus, the circularly permuted ligand is inserted within the recombinant PE molecule after about amino acid 607 and is followed by amino acids 604-613 of domain III. The circularly permuted ligand may also be inserted into domain Ib to replace sequences not necessary for toxicity. Debinski et al. Mol. Cell. Biol., 11: 1751-1753 (1991).

Detailed Description Text (32):
Circularly Permuted IL4-Pseudomonas Exotoxin Fusion Protein: Preparation and Biological Activity.

Detailed Description Paragraph Table (5):

SEQUENCE LISTING - (1) GENERAL INFORMATION: - (iii) NUMBER OF SEQUENCES: 72 - (2) INFORMATION FOR SEQ ID NO:1: - (i) SEQUENCE CHARACTERISTICS: #acids (A) LENGTH: 614 amino (B) TYPE: amino acid (C) STRANDEDNESS: (D) TOPOLOGY: linear - (ii) MOLECULE TYPE: protein - (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..614 #/note= "native Pseudomonas exotoxin (PE)" - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1: - Met Ala Glu Glu Ala Phe Asp Leu Trp Asn Gl - #u Cys Ala Lys Ala Cys # 15 - Val Leu Asp Leu Lys Asp Gly Val Arg Ser Se - #r Arg Met Ser Val Asp # 30 - Pro Ala Ile Ala Asp Thr Asn Gly Gln Gly Va - #l Leu His Tyr Ser Met # 45 - Val Leu Glu Gly Gly Asn Asp Ala Leu Lys Le - #u Ala Ile Asp Asn Ala # 60 - Leu Ser Ile Thr Ser Asp Gly Leu Thr Ile Ar - #g Leu Glu Gly Gly Val #80 - Glu Pro Asn Lys Pro Val Arg Tyr Ser Tyr Th - #r Arg Gln Ala Arg Gly # 95 - Ser Trp Ser Leu Asn Trp Leu Val Pro Ile Gl - #y His Glu Lys Pro Ser # 110 - Asn Ile Lys Val Phe Ile His Glu Leu Asn Al - #a Gly Asn Gln Leu Ser # 125 - His Met Ser Pro Ile Tyr Thr Ile Glu Met Gl - #y Asp Glu Leu Leu Ala # 140 - Lys Leu Ala Arg Asp Ala Thr Phe Phe Val Ar - #g Ala His Glu Ser Asn 145 1 - #50 1 - #55 1 - #60 - Glu Met Gln Pro Thr Leu Ala Ile Ser His Al - #a Gly Val Ser Val Val # 175 - Met Ala Gln Thr Gln Pro Arg Arg Glu Lys Ar - #g Trp Ser Glu Trp Ala # 190 - Ser Gly Lys Val Leu Cys Leu Leu Asp Pro Le - #u Asp Gly Val Tyr Asn # 205 - Tyr Leu Ala Gln Gln Arg Cys Asn Leu Asp As - #p Thr Trp Glu Gly Lys # 220 - Ile Tyr Arg Val Leu Ala Gly Asn Pro Ala Ly - #s His Asp Leu Asp Ile 225 2 - #30 2 - #35 2 - #40 - Lys Pro Thr Val Ile Ser His Arg Leu His Ph - #e Pro Glu Gly Gly Ser # 255 - Leu Ala Ala Leu Thr Ala His Gln Ala Cys Hi - #s Leu Pro Leu Glu Thr # 270 - Phe Thr Arg His Arg Gln Pro Arg Gly Trp Gl - #u Gln Leu Glu Gln Cys # 285 - Gly Tyr Pro Val Gln Arg Leu Val Ala Leu Ty - #r Leu Ala Ala Arg Leu # 300 - Ser Trp Asn Gln Val Asp Gln Val Ile Arg As - #n Ala Leu Ala Ser Pro 305 3 - #10 3 - #15 3 - #20 - Gly Ser Gly Gly Asp Leu Gly Glu Ala Ile Ar - #g Glu Gln Pro Glu Gln # 335 - Ala Arg Leu Ala Leu Thr Leu Ala Ala Ala Gl - #u Ser Glu Arg Phe Val # 350 - Arg Gln Gly Thr Gly Asn Asp Glu Ala Gly Al - #a Ala Asn Ala Asp Val # 365 - Val Ser Leu Thr Cys Pro Val Ala Ala Gly Gl - #u Cys Ala Gly Pro Ala # 380 - Asp Ser Gly Asp Ala Leu Leu Glu Arg Asn Ty - #r Pro Thr Gly Ala Glu 385 3 - #90 3 - #95 4 - #00 - Phe Leu Gly Asp Gly Gly Asp Val Ser Phe Se - #r Thr Arg Gly Thr Gln # 415 - Asn Trp Thr Val Glu Arg Leu Leu Gln Ala Hi - #s Arg Gln Leu Glu Glu # 430 - Arg Gly Tyr Val Phe Val Gly Tyr His Gly Th - #r Phe Leu Glu Ala Ala # 445 - Gln Ser Ile Val Phe Gly Gly Val Arg Ala Ar - #g Ser Gln Asp Leu Asp # 460 - Ala Ile Trp Arg Gly Phe Tyr Ile Ala Gly As - #p Pro Ala Leu Ala Tyr 465 4 - #70 4 - #75 4 - #80 - Gly Tyr Ala Gln Asp Gln Glu Pro Asp Ala Ar - #g Gly Arg Ile Arg Asn # 495 - Gly Ala Leu Leu Arg Val Tyr Val Pro Arg Se - #r Ser Leu Pro Gly Phe # 510 - Tyr Arg Thr Ser Leu Thr Leu Ala Ala Pro Gl - #u Ala Ala Gly Glu Val # 525 - Glu Arg Leu Ile Gly His Pro Leu Pro Leu Ar - #g Leu Asp Ala Ile Thr # 540 - Gly Pro Glu Glu Glu Gly Gly Arg Leu Glu Th - #r Ile Leu Gly Trp Pro 545 5 - #50 5 - #55 5 - #60 - Leu Ala Glu Arg Thr Val Val Ile Pro Ser Al - #a Ile Pro Thr Asp Pro # 575 - Arg Asn Val Gly Gly Asp Leu Asp Pro Ser Se - #r Ile Pro Asp Lys Glu # 590 - Gln Ala Ile Ser Ala Leu Pro Asp Tyr Ala Se - #r Gln Pro Gly Lys Pro # 605 - Pro Arg Glu Asp Leu Lys 610 - (2) INFORMATION FOR SEQ ID NO:2: - (i) SEQUENCE CHARACTERISTICS: #acids (A) LENGTH: 129 amino (B) TYPE: amino acid (C)